

- 2 -

LISTING OF THE CLAIMS

Claim 1 (**canceled**)

Claim 2 (**currently amended**) A method for the production of a single heavy chain antibody in a transgenic non-human mammal comprising expressing a heterologous VHH heavy chain locus in that mammal specifically in B cells in response to antigen challenge wherein the VHH heavy chain locus is integrated into the non-human mammal's genome and said VHH heavy chain locus comprises:

(a) at least one VHH exon, at least one~~[[D]]~~ D exon and at least one~~[[J]]~~ J exon, wherein the VHH exon, the D exon and the J exon are capable of recombining to form VDJ coding sequence, and wherein the VHH exon comprises a naturally occurring VHH coding sequence, and

(b) a constant heavy chain region comprising at least one constant heavy chain gene, wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain,

(c) a locus control region (LCR) providing for expression of the VHH heavy chain locus specifically in B cells

said method comprising:

- 1) immunizing said mammal with an antigen and
- 2) isolating single heavy chain antibody against said antigen ~~[[from said mammal]]~~.

Claim 3 (**canceled**)

Claim 4 (**canceled**)

- 3 -

Claims 5 – 6 (**canceled**)

Claim 7 (**currently amended**) The method of claim 2 or 41 wherein the VHH single heavy chain locus comprises a camelid VHH, at least one D exon of human origin and at least one J exon of human origin and a constant region of human origin.

Claim 8 (**canceled**)

Claim 9 (**canceled**)

Claim 10 (**currently amended**) The method of claim 2 or 41 wherein the constant heavy chain region comprises at least one constant region heavy chain gene which is of non-camelid origin.

Claim 11 (**previously presented**) The method of claim 10 wherein at least one constant region heavy chain gene is of human origin.

Claims 12 – 16 (**canceled**)

Claims 17 - 32 (**canceled**)

Claim 33 (**currently amended**) The method of claim 2 or 41 wherein the entire VHH single heavy chain locus is of camelid origin

Claims 34-36 (**canceled**)

Claims 37-38 (**canceled**)

Claim 39 (**currently amended**) The method according to claim 2 or 41 wherein the non-human mammal is a rodent.

Claim 40 (**canceled**)

Claim 41 (**currently amended**) A method for the production of a single heavy chain

- 4 -

antibody in a transgenic mouse comprising expressing a heterologous VHH heavy chain locus in [[that mammal]] the mouse specifically in B cells in response to antigen challenge wherein the VHH heavy chain locus in integrated into said mouse's genome and said VHH heavy chain locus comprises:

(a) at least one VHH exon, at least one-D exon and at least one-J exon, wherein the VHH exon, the D exon and the J exon are capable of recombining to form VDJ coding sequence, and wherein the VHH exon comprises a naturally occurring VHH coding sequence, and

(b) a constant heavy chain region comprising at least one constant heavy chain gene, wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain,

(c) a regulatory sequence providing for expression of the VHH heavy chain locus specifically in B cells

said method comprising:

- 1) immunizing said mammal with an antigen and
- 2) isolating single heavy chain antibody against said antigen [[from said mammal]].

Claim 42 (**canceled**)

Claim 43 (**new**) The method of claim 2 or 41 wherein said antibody is isolated using hybridoma technology.

Claim 44 (**new**) The method of claim 2 or 41 wherein said antibody comprises a variable region fragment and said variable region fragment is isolated using phage display.